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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,373	05/04/2005	Diego A. Gianolio	4830-13PUS	8655

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EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,373	GIANOLIO ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-30* is/are pending in the application.

4a) Of the above claim(s) *21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20 and 22-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9 pgs / 14 Oct 2004, 15 Jul 2005, 18 Apr 2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is the national stage entry of PCT/ PCT/US03/11830, filed 17 Apr 2003; and claims benefit of provisional application 60/373,279, filed 17 Apr 2002.

Claims 20-30 are pending in the current application. Claim 21, drawn to non-elected inventions, are withdrawn. Claims 20 and 22-30 are examined on the merits herein.

However, the parent applications 60/373,279 upon which priority is claimed fail to provide adequate support under 35 U.S.C. 112 for the instant claim 23 of this application since the parent application is not seen to disclose the compounds:

1,1',1"-methylidynetrisaziridine;

1,1',1"-methylidynetris[2,2-dimethyl]-aziridine;

1,1'-[2-(1-aziridinylmethyl)-1,3-propanediyl]bis-aziridine;

1-aziridinepropanoic acid, 2,2-bis[[3-(1-aziridinyl)-1-oxopropoxylmethyl)-1,3-propanediyl ester;

1-Aziridinepropanoic acid, 2-propyl-, 2-(hydroxymethyl)-2-[[1-oxo-3-(2-propyl-1-aziridinyl)propoxy]methyl]-1,3-propanediyl ester; or

1-aziridinepropanoic acid, 2,2-dimethyl-, 2-[[3-(2,2-dimethyl-1-aziridinyl)-1-oxopropoxylethyl]-2-(hydroxymethyl)-1,3-propanediyl ester

of the dependent claim 23. Written description for the remaining compounds in claim 23 may be found in page 9, lines 15-21, however no support is found for the above listed compounds. Thus, the filing date of instant claim 23 is deemed to be the PCT filing date of the instant application, 17 Apr 2003. The filing date of instant claims

20 and 22-30 is deemed to be the filing date of the parent provisional application, 17 Apr 2002. If applicant disagrees, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the earlier priority applications. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

Election/Restrictions

Applicant's election of the Group V, claim 20, in the reply filed on 18 Apr 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

New claims 22-29, drawn to the invention of Group V, are examined herein.

Specification

The abstract of the disclosure is objected to because of a minor informality: in line 4 there appears to be two periods following the ratio "1:5..". Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 20, 22 and 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins et al. (US Patent 6,096,728, issued 01 Aug 2000, cited in PTO-892) in view of Vanderhoff et al. (US Patent 6,214,331, issued 10 Apr 2001, provided by Applicant in IDS mailed 18 Apr 2008).

Collins et al. discloses the injection of hyaluronic acid derivatives to restore the damaged hyaluronic acid layer on the articular cartilage surface (column 3, lines 44-50), meeting limitations of instant claims 27-28. Collins et al. discloses the injection into the knees of a subject (column 38, line 37), meeting limitations of instant claim 29. Collins et al. discloses such conditions include osteoarthritis (column 3, lines 34), meeting

limitations of instant claim 30. Collins et al. discloses the use of crosslinked gels of hyaluronic acid (column 5, lines 48-51), specifically hyaluronic acid crosslinked with polyaziridyl compounds (column 6, lines 40-42), meeting limitations of instant claim 20. A gel, or a colloid in a more solid form than a sol, is synonymous with a gel slurry, a watery mixture of insoluble matter, because a colloid is a mixture of solid insoluble matter in a solution. Collins et al. discloses the use of hyaluronan with a molecular weight of $1x10^7$ (column 6, lines 11-15), meeting limitations of instant claim 26.

Collins et al. does not specifically disclose the ratio of hyaluronan to aziridine is 1:1 to 1:10 (instant claim 20). Collins et al. does not specifically disclose the polyaziridyl crosslinking compound pentaerythritol-tris-[beta(N-aziridinyl proprionate], a cross-linking agent that has three aziridines (instant claims 22 and 25).

Vanderhoff et al. teaches a polysaccharide polymer such as hyaluronic acid crosslinked with the polyaziridyl compound XAMA-7, or pentaerythritol-tris-[beta(N-aziridinyl proprionate] (column 8, lines 42-45 and spanning column 8, 55-67 and column 9, lines 1-2). Vanderhoff et al. teaches the selection of an appropriate crosslinking agent can readily be accomplished by those of skill in the art (column 8, lines 63-65). Vanderhoff et al. teaches the polysaccharide crosslinked with XAMA-7, a compound containing three aziridine groups, at a ratio of 7:4 (column 13, lines 17-20), corresponding to a ratio of polysaccharide to aziridine group of 1:1.7. Vanderhoff et al. teaches the crosslinked polymer is useful as a replacement composition in tissues in the bone, cartilage, and tendon (column 7, lines 15-18).

It would have obvious to one of ordinary skill in the art at the time of the invention to combine the invention disclosed by Collins et al. with the teaching of Vanderhoff et al. of the polyaziridyl crosslinking compound XAMA-7, or pentaerythritol-tris-[beta(N-aziridinyl proprionate], at a specific concentration of polysaccharide to aziridine group. Collins et al. teaches the use of hyaluronic acid crosslinked with polyaziridyl compounds. Both Collins et al. and Vanderhoff et al. are drawn to the use of the polymer as a replacement composition in tissues. One of ordinary skill in the art would have been motivated to combine Collins et al. with the teaching of Vanderhoff et al. because Vanderhoff et al. teaches it advantageously creates particles with a narrow size distribution with defined physical characteristics (Vanderhoff et al. column 4, lines 36-40).

Claims 20, 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins et al. (US Patent 6,096,728, issued 01 Aug 2000, cited in PTO-892) in view of Vanderhoff et al. (US Patent 6,214,331, issued 10 Apr 2001, provided by Applicant in IDS mailed 18 Apr 2008) as applied to claims 20, 22 and 25-30 above, and further in view of Coker et al. (US Patent 3,726,862, issued 10 Apr 1973, cited in PTO-892).

Collins et al. in view of Vanderhoff et al. teaches as above.

Collins et al. in view of Vanderhoff et al. does not specifically teach a polyfunctional crosslinking agent that has two aziridines, such as di[2-(1-aziridinyl)ethyl]adipate (instant claims 23 and 24).

Coker et al. teaches di[2-(1-aziridinyl)ethyl]adipate (column 4, lines 34-35) useful as curing agents for acid terminated polymers (column 4, lines 23-25). In the field of polymer science a crosslinking agent is a curing agent.

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the crosslinking agent of pentaerythritol-tris-[beta(N-aziridinyl proprionate] in the invention made obvious by Collins et al. in view of Vanderhoff et al. with the curing agent, or crosslinking agent, for acid terminated polymers of di[2-(1-aziridinyl)ethyl]adipate taught by Coker et al. It is *prima facie* obvious to substitute equivalents known in the prior art for the same purpose. An express suggestion to substitute one equivalent component for another is not necessary to render such substitution obvious, see MPEP 2144.06 II. On of ordinary skill in the art would have a reasonable expectation of success to substitute the crosslinking agent of pentaerythritol-tris-[beta(N-aziridinyl proprionate] in the invention made obvious by Collins et al. in view of Vanderhoff et al. with the curing agent, or crosslinking agent, for acid terminated polymers of di[2-(1-aziridinyl)ethyl]adipate taught by Coker et al. because Vanderhoff et al. teaches the selection of an appropriate crosslinking agent can readily be accomplished by those of skill in the art (Vanderhoff et al. column 8, lines 63-65).

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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